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Th1 immune response induced by Ipr1-PPE68 DNA vaccine in BALB/C mice model

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An effective tuberculosis (TB) vaccine could have a significant impact on the current TB pandemic. BCG has been used as a vaccine against tuberculosis for 90 years, but its immune effect is unstable. The RD1 region which is present in mycobacterium tuberculosis such as H37Rv but not in BCG and other attenuated or avirulent strains is relative with the virulence and immunogenicity. However, one of its products named PPE68 encoded by Rv3873 has noting to do with the virulence of RD1 region but closely correlates with antigen diversity and the mechanism of immune escape. Ipr1 (intracellular pathogen resistance 1)expressed in macrophage is located within the sst1(super-susceptibility to tuberculosis 1) of mouse. It has the function of mediating innate immunity and limiting the replication of MTB. In this study, the Ipr1-PPE68 co-expression plasmid (pBudce4.1/Ipr1-PPE68) was constructed successfully, and the expression of PPE68 and Ipr1 gene was detected by RT-PCR and Western blotting in the transfected macrophage RAW264.7. The BALB/c mice were immunized three times with the physiological saline, BCG, pBudce4.1, PPE68 DNA vaccine, Ipr1 DNA vaccine and Ipr1-PPE68 DNA vaccine, respectively. Mice were sacrificed two weeks after the last immunization, the level of IgG2a, IL-12, IL-4 and IFN-γ in serum was analyzed by ELISA. Specific proliferation of spleen lymphocytes and the quantity of CD4+ and CD8+T cells were detected with MTT assay and FCM respectively. The tissue slices of lungs and spleens were observed at the same time. The results showed that the specific lymphocyte proliferation of Ipr1-PPE68 DNA vaccine group, PPE68 DNA vaccine group and BCG group was higher than other control groups ($P < 0.05$). The level of IgG2a and IL-12 of Ipr1-PPE68 DNA vaccine group was higher than all other groups ($P < 0.05$). The level of IFN-γ of Ipr1-PPE68 DNA vaccine group and Ipr1 DNA vaccine group was higher than other control groups ($P < 0.05$). The level of IL-4 in all groups has no significant difference. Compared with BCG group, the percentage of CD4+ and CD8+T cells was increased in Ipr1-PPE68 DNA vaccine group, and CD4 + / CD8+ was decreased. The pathological examination showed that lung tissue of mice appears a little hyperemia in BCG group, while there was no obvious lesion in Ipr1-PPE68 DNA vaccine group. The study showed that Ipr1-PPE68 DNA vaccine could induce high level of Th1 immune response in mice which plays the most important role in anti-mycobacterial immunity in human and mouse. It provides an experimental basis for the research of protection effect of Ipr1-PPE68 DNA vaccine.

Biography

Chun Yang is the professor and director of department of pathobiology in Chongqing Medical University. She mainly engaged in the research of mycobacterium tuberculosis infection and immune. At present the main research work include the therapeutical effect of GLS/IL-12 recombinant vaccine on TB and the immune protection of PPE68 DNA vaccine and PPE-IPR1 DNA vaccine against the mycobacterium tuberculosis infection. Relevant results have published in Oligonuecleotides, Vaccine and INT J TUBERC LUNG DIS magazines.

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